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(54) Title: SYNERGISTIC COMBINATIONS OF MACROLIDE T-CELL MODULATOR OR IMMUNOSUPPRESSANT AND A RETINOID

(57) Abstract: Additive or synergistic combinations of a macrolide T-cell immunomodulator or immunosuppressant such as 33-epichloro-33-desoxyascomycin and a retinoid, such as etretinate, isotretinoin or tazarotene, optionally with a further pharmaceutically active agent, especially an antibacterial, are provided, which are useful in particular in the treatment of dermatological diseases such as eczema, atopic dermatitis, acne, psoriasis, skin aging, sun damage, post-peel erythema and stretch marks.

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP2004/003511

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/05 A61K31/436 A61P17/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/098376 A1 (THE REGENTS OF THE UNIVERSITY OF MICHIGAN; KANG, SEWON; VOORHEES, JOHN) 12 December 2002 (2002-12-12) claim 1	1,3,4
X	KOKELJ F ET AL: "Efficacy of cyclosporine plus etretinate in the treatment of erythrodermic psoriasis (three case reports)." JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY : JEADV. SEP 1998, vol. 11, no. 2, September 1998 (1998-09), pages 177-179, XP002315676 ISSN: 0926-9959	3
Y	page 179, paragraph entitled "2. Discussion"	1-6



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

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14/02/2005

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International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHAIDEMENOS G C ET AL: "Combination of cyclosporin A and acitretin in resistant erythrodermic psoriasis" JEADV. JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 11, September 1998 (1998-09), pages S290-S291, XP004556159 ISSN: 0926-9959	3
Y	S290-S291 P446	1-6
X	TUYP E ET AL: "COMBINATION THERAPY FOR PSORIASIS WITH METHOTREXATE AND ETRETINATE" JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY, vol. 14, no. 1, 1986, pages 70-73, XP009043274 ISSN: 0190-9622	3
Y		1-6
Y	SINGH F ET AL: "ORAL TAZAROTENE AND ORAL PIMECROLIMUS: NOVEL ORAL THERAPIES IN DEVELOPMENT FOR PSORIASIS" JOURNAL OF DRUGS IN DERMATOLOGY, STRATEGIC COMMUNICATION IN DERMATOLOGY, NEW YORK, NY, US, vol. 3, no. 2, March 2004 (2004-03), pages 141-143, XP009039266 ISSN: 1545-9616 page 142-143	1-6
P,X	CONNELLY E A ET AL: "Treatment of facial angiofibromas with topical pimecrolimus and tazarotene gel." JOURNAL OF INVESTIGATIVE DERMATOLOGY, vol. 121, no. 1, July 2003 (2003-07), page 0030, XP009043277 & INTERNATIONAL INVESTIGATIVE DERMATOLOGY 2003 : JOINT MEETING OF THE EUROPEAN SOCIETY FOR DERMATOLOGI; MIAMI BEACH, FLORIDA, USA; APRIL 30-MAY 04, 2003 ISSN: 0022-202X abstract 0030	3

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP2004/003511

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy: Although claim 3 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

### Information on patent family members

PCT/EP2004/003511

Form PCT/ISA/210 (patent family annex) (January 2004)